REMARKS

Claims 16, 18-20, 22-30 and 32-36 are pending and under examination in the subject application. Applicants have not added, amended or canceled any claims. Accordingly, claims 16, 18-20, 22-30 and 32-36 are still pending and under examination.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 16, 18-20, 22-30 and 32-36 under 35 U.S.C. §112, first paragraph.

In response, applicants respectfully traverse.

Briefly, the invention provides a method for reducing vascular tissue injury during reperfusion of an ischemic tissue in a subject which comprises contacting the vascular tissue within the ischemic tissue with a nucleic acid which inhibits expression of Early Growth Response Factor-1 (Egr-1) protein in the vascular tissue so as to reduce vascular tissue injury in the ischemic tissue during reperfusion. The invention also provides a method for reducing ischemic damage to tissue being transplanted into a subject, which comprises contacting the cells of the tissue with a nucleic acid that inhibits Early Growth Response Factor-1 (Egr-1) *ex vivo* prior to the tissue's transplantation into the subject.

The Examiner concedes that the specification is enabling for a method for reducing ischemic damage to a lung tissue being transplanted into a subject comprising contacting the lung tissue *ex vivo* with SEQ ID NO. 1. However, the Examiner asserts that the

specification does not enable a method for reducing ischemic damage to a tissue being transplanted into a subject comprising contacting the tissue with any nucleic acid that inhibits the expression of Egr-1. While the Examiner acknowledges that the specification shows increased arterial oxygenation and survival times of rats transplanted with preserved lungs with Egr-1 antisense (SEQ. ID. NO: 1), the Examiner alleges that the unpredictability of the art of nucleic acid therapy in general would require one skilled in the art to perform undue experimentation in order to practice the claimed invention.

Applicants maintain that the instant specification does enable a person skilled in the relevant art to use the invention commensurate in scope with the claims. Specifically, applicants assert that, based on the art at the time of filing, identifying additional nucleic acids (i.e. antisense) capable of inhibiting Egr-1 expression would not have required undue experimentation. In support of this position, applicants direct the Examiner's attention to Smith et al. (Rational selection of antisense oligonucleotide sequences" Euro. J. Pharma. Sci. 11: 191-198 (2000)), attached hereto as **Exhibit A.**

Smith et al. describes several procedures for identifying optimal antisense oligonucleotide sequences. Applicants maintain that one skilled in the relevant art, based on the specification and Smith et al., would be able to select the most favorable procedure(s) for identifying other nucleic acids that would inhibit Egr-1 expression without undue experimentation.

Again, the Examiner has conceded that the specification *is* enabling

for a method of reducing ischemic damage to lung tissue being transplanted into a subject comprising contacting the tissue with SEQ. ID. No: 1 *ex vivo*. The existence of this working example (SEQ. ID. NO: 1), together with Smith et al. and the remainder of the specification, only underscores applicants' position that no undue experimentation would be required to identify additional nucleic acids for use in the claimed invention.

Throughout the Final Office Action, the Examiner alleges that the specification is not enabling for "an *in vivo* method for reducing ischemic damage to a tissue being transplanted into a subject comprising contacting the tissue with any nucleic acid which inhibits the expression of Egr-1." Applicants note that no current claim is limited to such an invention, but rather understand the Examiner's rejection as directed to claim 16. This claim provides a method for reducing vascular tissue injury during reperfusion of an ischemic tissue in a subject which comprises contacting the vascular tissue within the ischemic tissue with a nucleic acid which inhibits expression of Early Growth Factor-1 (Egr-1) protein in the vascular tissue. Specifically, the Examiner alleges that the specification provides no particular guidance or direction for addressing the problems of targeting, permanence and quantity of expression of the gene in question, immunogenicity, etc., for nucleic acid/antisense targeting of Egr-1 *in vivo*.

In response, applicants respectfully traverse.

Applicants maintain that one skilled in the art would be able to practice the *in vivo* method of claim 16 without undue experimentation. Specifically, applicants assert that, based on

the instant specification and the art at the time of filing, one skilled in the art would be able to deliver an effective amount of antisense to a desired location within a subject in order to inhibit RNA expression *in vivo* without undue experimentation. In support of their position, applicants direct the Examiner's attention to Morishita et al. ("Antisense Oligodeoxynucleotide Inhibition of Vascular Angiotensin-Converting Enzyme Expression Attenuates Neointimal Formation - Evidence for Tissue Angiotensin-Converting Enzyme Function," Arterioscler. Thromb. Vasc. Biol. 20: 915-922 (2000), attached hereto as **Exhibit B.**

On page 916, Morishita et al. describe the *in vivo* transfer of antisense angiotensin-converting enzyme ("ACE") oligonucleotides into the carotid artery of a rat which resulted in significant reduction of vascular ACE activity. Specifically, a cannula was used to infuse an HVJ-liposome complex (200 µL, 10 µmol/L ODN with or without HMG-1 and RNase H) into the common carotid artery of a rat for 10 minutes. One week after infusion, vascular ACE activity was measured, showing a significant reduction in ACE activity in rats infused with antisense phosphorothioate ACE ODN compared to rats infused with sense ODN (see page 918 and Figure 2). Accordingly, applicants maintain that, as demonstrated by Morishita et al., procedures were known at the time of filing for the effective *in vivo* delivery of antisense in order to inhibit gene expression.

In view of the above remarks, applicants maintain that claims 16, 18-20, 22-30 and 32-36 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Summary

In view of the remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
Tel. No. (212) 278-0400

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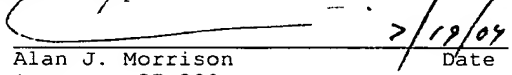

2/19/07
Alan J. Morrison Date
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